

REMARKS

Claims 27, 28, 38-50 and 52 are pending. The Examiner has treated Claim 51 as being cancelled, which was not the case. However, in order to expedite prosecution, claim 51 has now been cancelled, without disclaimer. Reconsideration and allowance of the are respectfully requested.

Claims 39-41, 27, 28, 38, 42-45, 47 and 52 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The claims have been amended to overcome these rejections. In particular, claim 27 now specifies that the plant characteristic produced by the inserted gene can be used to prevent the production of seeds that are capable of developing into mature plants, supported on page 7, lines 25-34 of the specification. Claim 52 has been amended to remove references to "genetic inhibitor" and "plant development". In claims 39-42 the recombinase has been clarified as to its function, i.e. it functions as a disrupter, providing antecedent basis for "recombinase" later in the claim.

Claims 27, 28, 38, 42, 43, 44, 45, 47, and 52 are objected to as being improperly multiply dependent. These claims have been amended to make them properly multiply dependent. Finally, the misspelling of "lac" in claim 44 has been rectified.

The examiner has requested a certified copy of GB 9276151.2, filed July 29, 1992. A certified copy has been requested and will be submitted shortly. However, this application also claims priority from PCT/GB93/01605, filed July 29, 1993. Certified copies need not be normally provided during the nation phase of a PCT application. A request for a corrected Official Filing Receipt is submitted herewith.

Claims 27, 28, 39, 40, 42, 43, 45, 47, 48, 49, 50, and 52 are rejected under 35 U.S.C. §102(e) as being anticipated by Oliver *et al.* (U.S. Pat. No. 5,723,765).

The Applicants respectfully disagree because Oliver *et al.* was filed on June 7, 1995, and claims priority to August 1, 1994. The current application is a continuation of application number 08/374,783, which claims domestic priority from PCT/GB93/01605, filed July 29, 1993. Consequently, the Oliver *et al.* patent cannot be cited as prior art.

Claim 46 is rejected under 35 U.S.C. §102(e) as being anticipated by Williams *et al.* (U.S. Pat. No. 5,750,867).

Williams *et al.* relates to the production of male-sterile plants that are used to produce viable hybrid seed. Therefore, it is clearly directed to the field of hybrid seed production (see, for example, column 13, lines 1 to 17; column 5, lines 17 to 25). As amended, the chemical

inducer of the present invention controls whether the plant produces seeds capable of developing into a mature plant. In contrast to Williams *et al.* the claimed expression system is drawn to using an inducible promoter to **prevent** viable seeds from being produced. This property allows plants to be confined to a particular growing area and preventing them from persisting in the wild (see paragraph bridging pages 1 and 2 of the specification). This type of control is not possible with the construct of Williams *et al.*

The Examiner is correct in stating that the Williams *et al.* patent discloses that the barnase gene can be used in male-sterility DNA. However, these male-sterile plants are specifically intended to be pollinated by other plants, thus producing hybrid seeds that will develop into mature plants. The current invention is not directed to producing seeds that will develop into mature plants and indeed is directed to the opposite, i.e., preventing seeds that will develop into mature plants (albeit in a reversible manner using an inducible promoter). For example, as discussed on page 8 (last full paragraph) of the present application, early seedling growth can be inhibited, which prevents the seeds from maturing and producing viable seeds.

Applicants submit that this application is in condition for allowance. A timely Notice to that effect is respectfully requested. Should questions relating to patentability remain, the Examiner is invited to contact the undersigned to discuss the same.

Respectfully submitted,

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Enclosure: Appendix

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Cancel claim 51.

27. (Twice Amended) An expression system as claimed in **[any of]** claims **[39-41]** 39, 40, or 41, wherein the plant characteristic produced by said inserted gene can be used to prevent the production of seeds capable of developing into mature plants [controlled by the system is essential to plant growth, whereby the presence or absence of the exogenous chemical inducer induces a response selected from the group consisting of growth to maturity, retarded growth and growth cessation at said predetermined stage].

28. (Amended) An expression system as claimed in **[any of]** claims **[39-41]** 39, 40, or 41, wherein said inducible promoter sequence is functionally linked to and controls a repressor protein gene and in which the disrupter gene promoter includes an operator sequence recognized by said repressor protein, so that in the presence of the inducer the repressor protein is produced which interacts with the operator sequence disabling the plant developmental gene promoter and inhibiting expression of the disrupter gene.

38. (Twice Amended) An expression system as claimed in **[any of]** claims **[39-41]** 39, 40, or 41, wherein said plant developmental gene sequence is a promoter selected from the group consisting of the gene promoters of malate synthase genes, germin genes, glyoxysomal enzyme genes, aleurone layer genes and carboxypeptidase genes.

39. (Twice Amended) An expression system functional in a plant comprising:

- (e) an inducible promoter sequence responsive to the presence or absence of an exogenous chemical inducer;
- (f) either
 - (iii) a gene encoding a repressor protein under control of said inducible promoter; or

- (iv) a gene encoding an inhibitor of the recombinase disrupter specified at (d) below under control of said inducible promoter;
- (g) a plant developmental gene promoter sequence activated at a predetermined stage of plant development, which, in the case of (b)(i) above, includes an operator sequence recognized by said repressor protein, the presence of which inactivates said plant developmental gene promoter; and
- (h) a gene encoding a recombinase that functions as a disrupter of a plant characteristic produced by an inserted gene, the gene encoding the recombinase being under the control of said plant developmental gene promoter sequence, and the recombinase being adapted to excise a nucleotide sequence flanked by recombinase recognition sequences,

wherein the recombinase gene is the FLP gene of the 2 micron plasmid of *Saccharomyces cerevisiae* and the recognition sequences are the FRT sequences which flank all or part of the inserted gene or its regulatory elements, wherein the inserted gene is a gene encoding a predetermined characteristic introduced into the plant by a recombinant DNA method, and

wherein the presence or absence of the exogenous chemical inducer controls whether said characteristic is displayed in the plant.

40. (Twice Amended) An expression system functional in a plant comprising:

- (e) an inducible promoter sequence responsive to the presence or absence of an exogenous chemical inducer;
- (f) either
 - (iii) a gene encoding a repressor protein under control of said inducible promoter; or
 - (iv) a gene encoding an inhibitor of the recombinase disrupter specified at (d) below under control of said inducible promoter;
- (g) a plant developmental gene promoter sequence activated at a predetermined stage of plant development, which, in the case of (b)(i) above, includes an operator sequence recognized by said repressor protein, the presence of which inactivates said plant developmental gene promoter; and

- (h) a gene encoding a recombinase that functions as a disrupter of a plant characteristic produced by an inserted gene, the gene encoding the recombinase being under the control of said plant developmental gene promoter sequence, and the recombinase being adapted to excise a nucleotide sequence flanked by recombinase recognition sequences, wherein the recombinase gene is the *Cre* gene of bacteriophage P1 and its recognition sequence or the *lox* sequences which flank all or part of the inserted gene or its regulatory elements, wherein the inserted gene is a gene encoding a predetermined characteristic introduced into the plant by a recombinant DNA method, and
- wherein the presence or absence of the exogenous chemical inducer controls whether said characteristic is displayed in the plant.

41. (Twice Amended) An expression system functional in a plant comprising:

- (e) an inducible promoter sequence responsive to the presence or absence of an exogenous chemical inducer;
- (f) either
 - (iii) a gene encoding a repressor protein under control of said inducible promoter; or
 - (iv) a gene encoding an inhibitor of the recombinase disrupter specified at (d) below under control of said inducible promoter;
- (g) a plant developmental gene promoter sequence activated at a predetermined stage of plant development, which, in the case of (b)(i) above, includes an operator sequence recognized by said repressor protein, the presence of which inactivates said plant developmental gene promoter; and
- (h) a gene encoding a recombinase that functions as a disrupter of a plant characteristic produced by an inserted gene, the gene encoding the recombinase being under the control of said plant developmental gene promoter sequence, and the recombinase being adapted to excise a nucleotide sequence flanked by recombinase recognition sequences, wherein the recombinase gene is the Activator transposase of *Zea mays*,

wherein the presence or absence of the exogenous chemical inducer controls whether said characteristic is displayed in the plant.

42. (Amended) An expression system as claimed in **[any of] claims [39-41] 39, 40, or 41**, wherein the inducible promoter is the promoter of the gene encoding the 27 **[kd]** kDa protein of glutathione-S-transferase II.

43. (Amended) An expression system as claimed in **[any of] claims [39-41] 39, 40, or 41**, wherein said inducible promoter comprises the promoter of the *AlcA* gene, the system further comprising a gene capable of expressing the *AlcR* protein *alcA* and *alcR* being obtainable from *Aspergillus*.

44. (Amended) An expression system as claimed in **[any of] claims [39-41] 39, 40, or 41**, which comprises a repressor protein gene, wherein said repressor protein gene encodes the *lac* **[lacc]** repressor or a repressor used by 434, P22 or *lambdabacteriophages*.

45. (Amended) An expression system as claimed in **[any of] claims [39-41] 39, 40, or 41**, which comprises a repressor protein gene, wherein the repressor protein encoded by said repressor protein gene is the *tet* repressor.

46. (Twice Amended) An expression system functional in a plant comprising:

- (e) an inducible promoter sequence responsive to the presence or absence of an exogenous chemical inducer;
- (f) a gene encoding a protein inhibitor of barnase [specified at (d) below] and containing the coding region of the *barstar* gene, under control of the said inducible promoter;
- (g) a plant developmental gene promoter sequence activated at a predetermined stage of plant development;
- (h) a disrupter gene which encodes barnase, under the control of the plant developmental gene promoter sequence;

whereby the presence or absence of the exogenous chemical inducer controls whether [barnase disrupts cell survival in] the plant produces seed capable of developing into a mature plant.

47. (Twice Amended) An isolated plant genome transformed via an expression system as claimed in **[any of] claims [39-41] 39, 40, or 41**.

48. (Amended) An isolated plant having transformed genome as claimed in claim 47.

49. (Amended) An isolated plant part having a transformed genome as claimed in claim 47.

50. (Amended) An isolated plant cell having a transformed genome as claimed in claim 47.

52. (Amended) A plant or seed engineered to comprise the expression system of claims 39, 40, or 41 **[any of claims 39-41, which is incapable of growing to maturity comprising a genome which includes a genetic inhibitor of seed germination or plant development, the activity of said inhibitor being regulatable by application of said exogenous chemical inducer]**.